Evaluation the helicobacter pylori infection in asthmatic children compared to control group

Original Article

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Abstract:

Background: Asthma is a highly prevalent chronic respiratory disease in children. Moreover, the underlying causes of asthma exacerbation are important because they are effective in controlling and preventing asthma. The aim of this study was to evaluate the helicobacter pylori infection in controlled and uncontrolled asthmatic children compared to healthy children.

Methods: This case- control study was done on 120 children aged 6-14 years with moderate to severe asthma. Diagnosis of asthma was performed according to GINA criteria with respect to the history and clinical examination. In addition, 120 healthy children without asthma were considered as the control group. Helicobacter pylori stool antigen test was evaluated for all patients. In addition to the above information, age, sex, duration of asthma and gastrointestinal symptoms were also recorded for each patient. Data were analyzed using SPSS15, Chi-square and Fisher's exact test and T-test.

Results: The mean age of children in the asthmatic and healthy children was 8.3±2 and 8.5±2.3, respectively (p=0.479). Totally, 57.5% and 58.3% of children were boys in the control group, and in asthmatic group, respectively. Thirty percent of children in the control group and 8.3% of children with asthma were H. pylori positive (p=0.000). Mean duration of asthma in children with H. pylori positive (3.3±1.55) and H. pylori negative (3.33±1.56) stool antigen showed no significant difference (p=0.944).

Conclusions: The results of this study indicated that there was an inverse relation between helicobacter pylori infection and asthma.

Keywords: Asthma, child, helicobacter pylori.

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Introduction:

Asthma is one of the most common chronic respiratory diseases and its prevalence has been increased in the last decade [1] The main trigger that causes asthma including allergens, pharmaceutical, environmental, occupational, infectious diseases, exercise and emotional factors [2]. Recently, the association of asthma with H. pylori infection is considered [3]. Helicobacter pylori is a gram-negative, spiral and flagellate bacteria. Helicobacter pylori colonizes the human stomach. [4] H. Pylori is usually acquired in childhood. Age and low socioeconomic status are the main risk factors for the H. Pylori infection, and population density and poor health status in childhood are strong risk factors and, in some cases, the organism causes severe diseases such as peptic ulcer and stomach cancer.

In recent years, several extra-intestinal manifestations of H. Pylori are described [5, 6]. Various methods are used to detect Helicobacter pylori infection, which is divided into two categories invasive and non-invasive. Helicobacter pylori stool antigen test is one of the non-invasive methods, which is used due to the convenience, speed and patient acceptability. Several studies have been conducted to evaluate the diagnostic value of this test. Although the results of these studies are somewhat different, it seems that a large number of these studies have been generally considered this test as an appropriate diagnostic method [7-12].

In different studies, the sensitivity and specificity of this test were over 90% [7, 8].

Given the high prevalence of H. Pylori infection in Iran [3] especially in the North [1] and controversies about the role of H. Pylori in patients with asthma, the aim of the current study was to evaluate the Helicobacter pylori in children with asthma compared to control group and to determine the precise role of these microorganisms in controlling asthma.

Methods:

This case-control study was done on 120 children aged 6-14 years with moderate to severe asthma, who were referred to Amirkola Hospital as a tertiary referral children hospital in north of Iran, in 2013. Diagnosis of asthma was performed according to GINA criteria with respect to the history and clinical examination. Patients with at least one year duration of asthma were included in the case and patients without asthma were included in the control group. Children with asthma, according to GINA criteria [13] were divided into three levels of asthma control as control, partial control and uncontrolled asthma (table 1). One hundred and twentyhealthy children without asthma were considered as the control group. Exclusion criteria were bismuth usage, H2 receptor blockers and proton pump inhibitors during the past 2 weeks and a history of antibiotic use during the previous month. Informed consent was obtained from all parents of childrenin both groups. Helicobacter pylori stool antigen test was evaluated for all patients by Intex kit (Helicobacter pylori stool Antigen, HpSA, Switzerland). In addition to the above information, age, sex, duration of asthma and gastrointestinal symptoms were also recorded for each patient. Data were analyzed using SPSS15, Chi-square and Fisher's exact test and T-test and $p<0.05$ was considered significant.

Results:

The study was done on 120 children with asthma including 60 children with controlled asthma and 60 children with uncontrolled asthma, and 120 non-asthmatic children as a control group. The mean age of children with asthma and control groups was 8.3±2 and 8.5±2.3 years, respectively (p=0.479). The mean duration of asthma and FEV1 was 3.3±1.5 years and 75.1±4.9 %, respectively. Totally, 9 (7.5%) asthmatic patients used steroids, and the disease severity was mild and severe in 109 patients (90.8%) and11 patients (9.2%), respectively.

Other baseline characteristics of studied children are illustrated in Table 2. Distribution of positive samples in the asthmatic children (8.3%) was significantly lower than children in the control group (30%). Distribution of positive samples was significantly lower in the asthmatic children than that in the control group, based on both genders (Table 3). Distribution of positive samples was lower in the asthmatic children with uncontrolled and controlled asthma than the control group and was lower in controlled asthma compared to the uncontrolled asthmatic patients (Figure 1).

Table 1: Levels of asthma control (in 4 weeks) according to GINA criteria

Characteristic	Controlled	Partly controlled	Uncontrolled
Daytime symptoms	Twice or less per week	More than twice per week	three or more features of partly controlled asthma
Limitations of activities	None	Any	
Nocturnal symptoms	None	Any	
Need for rescue/"reliever" treatment	Twice or less per week	More than twice per week	
Lung function (PEF or FEV1)	Normal	< 80% predicted or personal best	

Table 2: Baseline characteristic of children in asthmatic and control groups

Variable		Control N (%)	Asthmatic N (%)	p-value
Sex	Male	69 (57.5)	70 (58.3)	1
	Female	51 (42.5)	50 (41.7)	
Chronic abdominal pain	No	116 (96.7)	110 (91.7)	0.167
	Yes	4 (3.3)	10 (8.3)	
History of bad breath	No	114 (95)	111 (92.5)	0.595
	Yes	6 (5)	9 (7.5)	
Nausea	No	120 (100)	119 (99.2)	1
	Yes	-	1 (0.8)	
Hematemesis	No	120 (100)	120 (100)	-
	Yes	-	-	
Melena	No	120 (100)	120 (100)	-
	Yes	-	-	

Table 3. Distribution of H. Pylori antigen in stool of asthmatic and control groups based on gender

Sex	H. Pylori antigen	Control N (%)	Asthmatic N (%)	p-value
Male	Negative	49 (71)	65 (92.9)	0.001
	Positive	20 (29)	5 (7.1)	
Female	Negative	35 (68.6)	45 (90)	0.013
	Positive	16 (31.4)	5 (10)	

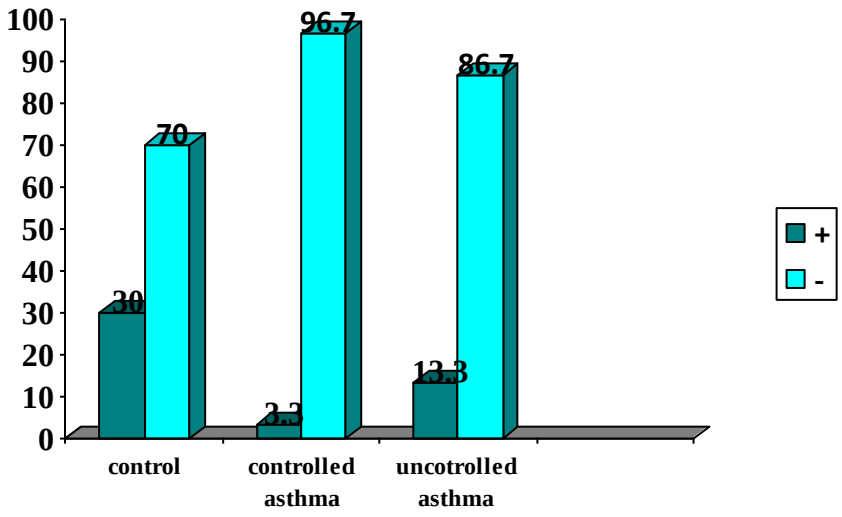

Figure 1: The relation between Helicobacter pylori infection and asthma control in children (p=0.000)

Discussion:

The aim of the present study was to evaluate the Helicobacter pylori infection in asthmatic children compared to control group in order to meticulously determine the role of this microbe in controlling asthma. The results suggested that 30% of normal children were infected by Helicobacter pylori while it was only 8.3% in asthmatic children ($p<0.05$). In other words, a significant inverse relationship was observed between Helicobacter pylori infection and asthma in children. A study of Pedulla et al. in Italy represented that the prevalence of Helicobacter pylori seropositivity was higher in children with nonatopic

asthma than in those with atopic asthma [14], which is similar to the present study. A cohort study conducted by Amberbir et al. in Ethiopia showed that Helicobacter pylori infection reduced the risk of eczema [15].

Moreover, a study of Shiotani et al. stated that the prevalence of Helicobacter pylori was lower in people with allergies than in the control group [16].

Reibman et al. in the United States studied on 318 adults with asthma and 208 normal individuals as the control group. Their study illustrated an inverse relationship between asthma and Helicobacter pylori infection in the serological test. Even, the mean age of asthma onset in patients infected by Helicobacter pylori and non-infected individuals was 21 and 11, respectively ($p<0.05$). [17], which shows that in addition to having a relationship, it can affect the age of disease onset. This relationship has also been observed in a different way. In a study by Zevit et al. 6959 children aged 5-18 underwent urease test for Helicobacter pylori infection and physical examination for asthma. The rate of asthma in children with Helicobacter pylori positive and negative was 7.3% and 9.1% respectively ($p<0.05$).[18], which is consistent with the results of the present study. It seems that the presence of Helicobacter pylori can control asthma by the disruption of TH1/TH2 equilibrium. This is due to the following reasons: Asthma and allergies are accompanied by TH2 response and the relevant cytokines such as IL-4 and IL-5. Helicobacter pylori are accompanied by TH1 response and interferon-gamma and IL-12 production. The presence of Helicobacter pylori causes TH1/TH2 profile tend towards TH1 and decreases allergies and asthma [19].

However, some studies have reported contradictory results so that in a study of Karimi et al. (2013), 98 asthmatic children and 98 healthy children were investigated and urea breath test was performed to evaluate Helicobacter pylori infection. Urease test was positive in 18.36% and 23.6% of the asthmatic children and the control group, respectively ($p>0.05$) [3].

Holster et al. in the Netherlands suggested that the rate of Helicobacter pylori infection (presence of antibodies in serum) in the asthmatic children and control group was 7.1% and 9.4% respectively ($p>0.05$) [20].

Moreover, in a study of Ahmed et al. (2011) in Egypt, 30 asthmatic children and 30 normal children, who were the same in terms of gestational age and gender, were investigated. Seroprevalence of Helicobacter pylori infection was 46.7% and 33.3% in the asthmatic children and control group, respectively ($p>0.05$) [21].

In addition to the above-mentioned studies, Wang et al. in a meta-analysis study assessed the case-control studies that had investigated the relationship between Helicobacter pylori and asthma. Finally, 770 patients and 785 normal individuals were entered into this meta-analysis study and no significant relationship was observed between Helicobacter pylori and the risk of asthma [22]. The results showed that more extensive studies under more controlled conditions are needed to meticulously determine the relationship between Helicobacter pylori and asthma.

In the present study, the distribution of Helicobacter pylori stool antigen, according to disease duration in asthmatic children did not increase or decrease. On the other hand, no significant difference was observed between the mean duration of asthma in individuals with positive (3.3±1.56) and negative (3.33±1.56) stool antigen test results (P=0.944). Karimi et al. (2013) conducted a study on 98 asthmatic children and 98 healthy children and concluded that there was a significant difference between the duration of asthma and positive urease test in asthmatic children [3], which is inconsistent with the results of the present study.

One of the differences between the present study and most of the studies mentioned earlier was that the stool antigen was used in the former while the blood samples or urease test were used in the latter. Although, on the whole, serological methods are less sensitive compared to culture, they can be used because of their ease of use.

In conclusions, the results of this study indicated that there was an inverse relation between helicobacter pylori infection and asthma in children. This present study suggests that Helicobacter pylori infection may inhibit development of asthma and may play a role in reducing the risk of asthma.

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